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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/764,712	01/23/2004	Miles B. Brennan	11320/33	9189

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/764,712	BRENNAN ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-23* is/are pending in the application.

4a) Of the above claim(s) *12-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,11 and 15-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/04;3/04;6/04;*.5/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 4/20/2006.

The communication filed on 4/20/2006 is acknowledged and has been entered.

Claims 10-23 are currently pending and are addressed herein.

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 4/20/2006 is acknowledged. The traversal is on the ground(s) that Groups I, II, IV, V and VI share compounds that are structurally similar in that they all protein or peptide compounds having a peptide linkage bond and the compounds share a common utility. This is not found persuasive because although they may all be compounds having a peptide linkage bond, this is not sufficient to establish a common structure between all of the compounds encompassed by the different inventions. If having a peptide linkage bond was sufficient to establish common structure, then all possible molecules having a peptide linkage bond would be structurally related to the instant compounds. Furthermore, since the compounds are structurally and functionally distinct for the reasons of record, a separate search would be required for each group. This separate search constitutes an undue burden on the office to search all of the indicated groups together.

The requirement is still deemed proper and is therefore made FINAL.

Claims 12-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/20/2006.

Information Disclosure Statement

The information disclosure statements submitted on 1/2004, 3/2004, 6/2004, and 5/2005 are acknowledged. The submissions are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 112, first paragraph

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claim 10, 11, 15-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method to methods of treatment that encompasses the administration of ***any*** compound that is an antagonist of MSH biological activity. The claims specifically encompass administering a fragment of MSH that has MSH antagonist action, a homolog of MSH that has MSH antagonist action. Therefore, the claims encompass a genus of compounds comprising a very large number of molecules, possibly millions, considering every possible variant, fragment, homolog, (etc.) molecule having MSH antagonist activity encompassed by the claims.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient

description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (See MPEP 2100-164)

The written description guidelines note regarding such genus/species situations that "Satisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) Here, the application discloses the structures of peptide molecules having MSH biological function, but does not disclose any antagonists of MSH biological activity. Furthermore, there is no indication of any fragment of MSH polypeptide which would act as MSH antagonist, nor is any MSH homolog having MSH antagonist activity identified. Also the specification does not provide sufficient guidance such that one of skill in the art would be able to readily recognize the MSH fragments and homolog would have MSH antagonist activity and which would not.

Therefore, the claims fail to meet the written description requirement because the claims encompass molecules which are not sufficiently described in the specification.

Claims 10,11, 15-23 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

> *Wands* states on page 1404,
> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The invention is drawn to methods of treating insulin resistance or diabetes caused by insulin resistance by administering an antagonist of MSH biological activity to a patient. Therefore, the invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The claims are very broad with respect to the genus of MSH antagonist compounds encompassed by the claims. As indicated above, the claims encompass administering any antagonist of MSH activity. As such, the claims could potentially encompass thousands, if not millions of different compounds, including compounds that have yet to be discovered or created.

The unpredictability of the art and the state of the prior art

As indicated above, the claims are drawn to methods of treating insulin resistance or diabetes caused by insulin resistance by administering an antagonist of MSH biological activity to a patient. Therefore, in order for the claimed method to work in a predictable manner, the antagonists encompassed by the claims must be able to ameliorate the effects of insulin resistance (claims 10, 11, 15-19 and 21-23) and diabetes caused by insulin resistance (claim 20). However, the prior art teaches that agouti, an antagonist of MSH biological activity, actually increases a insulin resistance and a form of type II diabetes associated with insulin resistance.

For instance, WO 97/47316 (Lee et al.; cited by Applicants in the 3/2004 IDS) teaches,

> "The agouti protein is a gene product expressed in mice that is known to be involved in determining coat color, but also thought to play a role in obesity when its normal expression pattern is de-regulated an the protein is ubiquitously expressed... it has been observed that agouti antagonizes the MSH-induced activation of two melanocortin receptors." (see page 2, first paragraph)

> "Ectopic expression of the normal, wild-type, agouti protein in transgenic mice result in obesity, diabetes, and the yellow coat color commonly observed in spontaneous obese mutants." (see page 3, last paragraph)

> "Agouti has been reported to be a competitive antagonist of αMSH binding to the MC1-R and MC4-R in vitro and the authors speculated that ectopic expression of agouti may lead to obesity by antagonism of melanocortin receptors expressed outside the hair follicle. In this regard a number of theories have been proposed to account for the induction of obesity by ectopic expression of agouti. For example agouti protein expression skeletal muscle may result in insulin resistance, hyperinsulinemia and obesity via elevation of Ca^2+ levels..." (see page 4, lines 7-17).

Furthermore, Klebig et al. (PNAS 92:4728-4732; 1995) teaches that ectopic expression of the agouti gene in transgenic mice causes obesity, features of type II diabetes associated with insulin resistance, and yellow fur. Specifically, Klebig teaches, "Transgenic mice of both sexes

have yellow fur, become obese, and develop hyperinsulinemia." (See abstract). Klebig also teaches that agouti is an antagonist of αMSH activity (see page 4728, second column).

Therefore, the prior art indicates that antagonists of MSH activity are associated with increased obesity and diabetes associated with insulin resistance. As such, one of skill in the art would not expect the MSH antagonists to be able to treat insulin resistance without performing additional experimentation.

Working Examples and Guidance in the Specification

The specification and working examples disclose the production of a transgenic mouse that does not express the pomc gene. It is noted that the pomc gene is responsible for the expression of αMSH (e.g., see page 11). The specification indicates that the pomc knock-out mice are protected from the development of obesity-induced insulin resistance and that administration of MSH to the mice nearly normalizes the glucoregulatory response in mice (see Example 2, page 52). However, the specification does not disclose that any specific antagonists of MSH biological activity were identified, nor does it disclose that an antagonist of MSG biological activity was able to treat insulin resistance or diabetes associated with insulin resistance in any patient (including the knock-out mouse or a human subject).

Quantity of Experimentation

Considering that the prior art indicates that MSH antagonists (specifically agouti) increases insulin resistance and diabetes associates with insulin resistance, and in view of the limited working examples and guidance provided in the specification, additional experimentation would be required. The additional experimentation would amount to trial and error testing of

MSH antagonists for their ability to treat insulin resistance and diabetes associated with insulin resistance which would amount to an inventive step over the prior art.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the nature of the invention, the breadth of the claims, the unpredictable nature of the invention as recognized in the prior art, the limited amount of working examples and guidance provided, and the high degree of skill required to practice the invention, it is concluded that the specification does not provide an enabling disclosure for the instant claims. Therefore, additional experimentation is required before one of skill in the art could make and use the claimed invention. The amount of additional experimentation required to perform the broadly claimed invention is undue.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.